North Bay CIRM Shared Research Laboratory for Stem Cells and Aging

Grant Award Details

North Bay CIRM Shared Research Laboratory for Stem Cells and Aging

Grant Type: Shared Labs

Grant Number: CL1-00501-1.1

Investigator:

Name:	Xianmin Zeng
Institution:	Buck Institute for Age Research
Type:	PI

Award Value: $2,414,749

Status: Closed

Grant Application Details

Application Title: CIRM Shared Research Laboratory for Stem Cells and Aging

Public Abstract:

Age-related diseases of the nervous system are major challenges for biomedicine in the 21st century. These disorders, which include Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis and stroke, cause loss of neural tissue and functional impairment. Currently, there is no cure for these devastating neurological disorders. A promising approach to the treatment of age-related neurological disorders is cell therapy, i.e., transplantation of nerve cells into the brain or spinal cord to replace lost cells and restore function. Work in this field has been limited however, due to the limited availability of cells for transplantation. For example, cells from 6-10 human fetuses obtained 6-10 weeks post-conception are required for one patient with Parkinson's disease to undergo transplantation.

Human embryonic stem cells (hESCs) offer a potentially unlimited source of any cell type that may be required for cell replacement therapy, due to their remarkable ability to self-renew (they can divide indefinitely in culture) and to develop into any cell type in the body. In this proposal, we will build out approximately 3400 square feet of shared laboratory space within our existing research facility for hESC research, as well as approximately 2400 square feet for classroom facilities dedicated to training in hESC culture and manipulation. We seek to understand how hESCs differentiate into authentic, clinically useful nerve cells and will use novel molecular tools to examine the behavior of cells transplanted in animal models of human neurological disease. We will also need to develop a noninvasive method of following cells after transplantation and we propose to develop luciferase-tagged (light-emitting) hESC lines for in vivo animal imaging. In addition, we will use hESC-derived nerve cells to screen drug and chemical libraries for compounds that protect nerve cells from toxicity, and to develop in vitro disease models. We believe that these experiments are critical to enhancing our understanding of neurological diseases and providing the tools that will be necessary to move cell therapy to the clinic.

Before a hESC-based therapy can be developed, it is essential to train scientists to efficiently grow, maintain and manipulate these cells. We propose to teach four 5-day hands-on training courses – two basic and two advanced hESC culture courses per year – to California scientists free of charge. These courses will provide scientists with an understanding of hESC biology and will enable them to set up and conduct hESC research after completion of training.

In summary, the goal of this proposal is to provide over twenty investigators at the home institute and neighboring institutions with the ability to culture, differentiate, and genetically manipulate hESCs – including clinical-grade hESC lines – to develop diagnostic and therapeutic tools.

Statement of Benefit to California:	We propose to build a Shared Research Laboratory and offer a Stem Cell Techniques Course for over twenty principal investigators at the home institute and neighboring institutes working collaboratively on stem-cell biology and neurological diseases of aging. We propose to: 1) Purify nerve cells at different stages of maturation from human embryonic stem cells and to develop transplantation strategies in animal models that mimic human diseases, including Parkinson's disease, stroke and spinal cord injuries; 2) Screen drug and chemical libraries for reagents that protect nerve cells from toxicity and develop in vitro disease models using nerve cells generated from human embryonic stem cells; and 3) Assess the long-term integration and differentiation of transplanted cells using a non-invasive imaging system. We believe these experiments provide not only a blueprint for moving stem-cell transplantation for Parkinson's disease toward the clinic, but also a generalized plan for how stem-cell therapy can be developed to treat disorders like motor neuron disease (amyotrophic lateral sclerosis, or Lou Gehrig's disease) and spinal cord injury. As the only stem-cell research facility in California's 10-12 most northwest counties, we are uniquely positioned to extend the promised benefits of Proposition 71 to this large part of the state. The tools and reagents we develop will be made widely available to California researchers and we will select California-based companies for commercialization of any therapies that may result. We also hope that California-based physicians will be at the forefront of translating this promising avenue of research into clinical applications. Finally, we expect that the money expended on this research will benefit the California research and business communities, and that the tools and reagents we develop will help accelerate stem-cell research in California and worldwide.